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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/660,568	09/11/2000	David Ralph	UROC:014USD1	1840

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EXAMINER	
MCGARRY, SEAN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/660,568	RALPH ET AL.	
	Examiner	Art Unit	
	Sean R McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-26,64 and 65* is/are pending in the application.

4a) Of the above claim(s) *21-26 and 65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-20 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 9-20 and 64 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The instant invention is broadly drawn to the detection of disease markers expressed in peripheral blood. The scope includes the detection of markers for metastatic cancers including breast and prostate cancers. The specification, as filed, discloses 7 “markers” (nucleic acid sequences) associated with metastatic prostate cancer expressed in peripheral blood of prostate cancer patients. The specification also identifies IL-8 and IL-10 expression in peripheral blood to be associated with metastatic

prostate cancer. The specification provides no other examples of any other diseases that may be associated with these 7 species and further provides no other marker genes specifically associated with any particular gene for use in the instantly claimed invention.

With the exception of the markers indicated above the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides markers required to perform the instant methods regardless of the complexity or simplicity of the method of isolation. The instant specification does not provide "markers" other than those indicated above and one in the art, based on the structure of those would not be able to envision the structure (sequence) of any other "markers" (mRNA) that may be associated with the broad scope of diseases considered in the instant invention. Without a description of such markers, one in the art would not be able to produce primers or probes for any particular marker associated with any particular disease, for example. The specification further does not provide any other disease states that may be determined via the increase or decrease in expression of the 7 "markers" identified in the specification, for example.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable

due to lack of written description for the broad class. The specification provided only the bovine sequence.

University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an

adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

The instant specification provides guidance for one in the art to find markers, but does not describe a representative number to show possession of the claimed invention. The markers disclosed in the specification are associated with prostate cancer, which fails to provide a description of markers for breast cancer or any of the vast number of disease states that would be included in a group described as ""a human disease state". The instant specification has not provided an adequate written

description of any markers for any disease other than metastatic cancer (prostate). The specification fails to describe those marker sequences that the invention requires to be quantified, for example. The detection of IL-10 or SEQ ID NO: 49 have been shown to be associated with metastatic prostate cancer but the specification fails to describe what disease other than metastatic prostate cancer can be detected by quantifying IL-10 or SEQ ID NO: 49 in peripheral blood, for example. The specification fails to provide a correlation between the structure and function of IL-10 or SEQ ID NO: 49 and any other diseases that may be detected by quantification of their expression in peripheral blood, for example.

The instant invention is based on the detection of markers that are differentially expressed in the peripheral blood in a patient with a disease relative to expression in a normal subject. Although the instant specification provides methods of identifying such markers, a sufficient number of markers have not been described to show possession of the broad scope instantly claimed.

Claims 9-20 and 64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are rejected for those reasons set forth above.

Applicant's arguments filed 12/05/03 have been fully considered but they are not persuasive.

Applicant argues that the claimed invention is a method of detecting and is not a compound. The argument appears to be that since the compounds not described are not being claimed no rejection of lack of written description can be made. It wou8ld appear that such an argument would represent a semantic distinction without a difference since the compounds not described are clearly needed in order to practice the claimed method.

Applicant argues that method have been provided to identify markers. Again it is pointed out *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Since the markers of the instant invention are clearly needed to practice the invention and the scope of such markers have not been adequately described, the invention itself [ie a method of using the markers] has not been described.

Applicant argues that the case law cited based on a description of cDNA structure is irrelevant. It is noted that the markers contemplated are nucleic acids, and further it is asserted by the examiner that applicants' argument is irrelevant since the statute applies to all types of inventions.

Applicant appears to admit on page 8, of their response that the claimed invention may encompass the use of compositions not specifically identified or identified

in the claims. It is the position of the examiner that the compositions required to practice the claimed invention have not been specifically exemplified or identified in the specification either.

Applicant argues also that the invention is enabled and argues that written description and enablement are distinct and cite *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1114 (Fed. Cir. 1991). It is the position of the examiner, that although distinct, there is overlap within the written description, enablement and best mode requirements of 112, first paragraph. In the instant case there is clearly overlap since one in the art would require the use of markers that have not been described. One cannot use these markers in the claimed invention when such markers have not been described. Applicant merely provided a trial and error method of finding "markers" where no guidance for what might be the structure and to what diseases they might be related and how a "difference" (increase, decrease, how much of increase or decrease, miss expression, different tissues, temporal . . etc) in expression of such undisclosed structures is to be correlated with any particular disease. The combinations contemplated are astronomical and the guidance provided is limited to seven markers all related to one type of disease. One in the art has been left to *de novo* determine all of the correlations, without any specific guidance for any particular diseases. One in the art has not been provided any particular starting point for what they might look for as a marker, but is left to find such by trial and error experimentation where there has been no guidance provided such that one would know how or where to look for markers for any particular disease they might wish to detect or diagnose, for example.

Any rejection of record not repeated in this Official Action has been withdrawn.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (571) 272-0761. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SRM

SEAN McGARRY
PRIMARY EXAMINER
1635